

CLAIMS

1. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D-E, wherein

A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes an immunoglobulin constant region-like domain,

D comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a transmembrane domain, and

E comprises a nucleotide sequence of at least one fifth exon of a T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a cytoplasmic domain,

with the proviso that E does not comprise a nucleotide sequence selected from a group consisting of SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29 and SEQ ID NO:31.

2. The isolated nucleic acid of claim 1 which is a cDNA.

3. The isolated nucleic acid of claim 2 which comprises a coding region of the cDNA.

4. The isolated nucleic acid of claim 1, wherein the nucleotide sequence is derived from a T cell costimulatory molecule gene encoding B7-1.

5. The isolated nucleic acid of claim 4, wherein B7-1 is murine.

6. The isolated nucleic acid of claim 4, wherein B7-1 is human.

7. The isolated nucleic acid of claim 5, wherein E comprises a nucleotide sequence shown in SEQ ID NO:4.

8. The isolated nucleic acid of claim 5, wherein E comprises a nucleotide sequence encoding an amino acid sequence shown in SEQ ID NO:5.

5 9. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 and is encoded by a T cell costimulatory molecule gene having

at least one first exon encoding a first cytoplasmic domain comprising a nucleotide sequence selected from the group consisting of a nucleotide sequence of SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29 and SEQ ID NO:31, and

10 at least one second exon encoding a second cytoplasmic domain, wherein the isolated nucleic acid comprises a nucleotide sequence encoding the second cytoplasmic domain.

15 10. The isolated nucleic acid of claim 9 which comprises a coding region of a cDNA.

11. The isolated nucleic acid of claim 9 which does not comprise a nucleotide sequence encoding the first cytoplasmic domain.

20 12. The isolated nucleic acid of claim 9 wherein the T cell costimulatory molecule gene is B7-1.

13. The isolated nucleic acid of claim 12 wherein B7-1 is murine.

25 14. The isolated nucleic acid of claim 12 wherein B7-1 is human.

15. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:1.

30 16. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:3.

35 17. An isolated nucleic acid encoding a cytoplasmic domain derived from a protein which binds CD28 or CTLA4, the nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:4.

18. A recombinant expression vector comprising the nucleic acid molecule of claim 15.

5 19. A host cell which contains the recombinant expression vector of claim 18.

20. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D-E, wherein
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A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

15 B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes an immunoglobulin constant region-like domain,

20 D, which may or may not be present, comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a transmembrane domain, and

25 E, which may or may not be present, comprises a nucleotide sequence of at least one fifth exon of a T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a cytoplasmic domain,

with the proviso that A does not comprise a nucleotide sequence selected from a group consisting of SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39 and SEQ ID NO:41.

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21. The isolated nucleic acid of claim 20 which is a cDNA.

22. The isolated nucleic acid of claim 21 which comprises a coding region of the cDNA.

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23. The isolated nucleic acid of claim 20, wherein the nucleotide sequence is derived from a T cell costimulatory molecule gene encoding B7-2.

24. The isolated nucleic acid of claim 23, wherein B7-2 is murine.

25. The isolated nucleic acid of claim 23, wherein B7-2 is human.

5 26. The isolated nucleic acid of claim 24, wherein A comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:14.

27. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 and is encoded by a T cell costimulatory molecule gene having
at least one first exon encoding a first signal peptide domain comprising a nucleotide
10 sequence selected from the group consisting of a nucleotide sequence of SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37 SEQ ID NO:39 and SEQ ID NO:41, and
at least one second exon encoding a second signal peptide domain,
wherein the isolated nucleic acid comprises a nucleotide sequence encoding the second signal peptide domain.

15 28. The isolated nucleic acid of claim 27 which comprises a coding region of a cDNA.

29. The isolated nucleic acid of claim 27 which does not comprise a nucleotide
20 sequence encoding the first signal peptide domain.

30. The isolated nucleic acid of claim 27 wherein the T cell costimulatory molecule gene is B7-2.

25 31. The isolated nucleic acid of claim 30 wherein B7-2 is murine.

32. The isolated nucleic acid of claim 30 wherein B7-2 is human.

33. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4
30 comprising a nucleotide sequence shown in SEQ ID NO:12.

34. An isolated nucleic acid encoding a signal peptide domain derived from a protein which binds CD28 or CTLA4, the nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:14.

35 35. A recombinant expression vector comprising the nucleic acid molecule of claim 33.

36. A host cell which contains the recombinant expression vector of claim 35.

37. An isolated nucleic acid encoding a protein comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D, wherein

5 A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

 B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an
10 immunoglobulin constant region-like domain,

 C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes a transmembrane domain, and

 D comprises a nucleotide sequence of at least one fourth exon of a T cell
15 costimulatory molecule gene, wherein the at least one fourth exon encodes a cytoplasmic domain.

38. The isolated nucleic acid of claim 37 comprising a nucleotide sequence shown in SEQ ID NO:8.

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39. The isolated nucleic acid of claim 37 comprising a nucleotide sequence shown in SEQ ID NO:10.